In light of the above amendments and following discussions, applicants respectfully request that the outstanding rejections be withdrawn and the claims be allowed.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Claims 14 and 25 are pending and stand rejected. The Examiner has rejected the claim under 35 U.S.C. §112, first paragraph. The Examiner has acknowledged that the specification is enabling for a method of treating Sjögren's syndrome with a fragment available upon proteolysis of α-fodrin, wherein the fragment comprises SEQ ID NO.1. However, it is the Examiner's position that the specification is not enabling for muteins of the fragment or sequences that are "substantially similar" to the fragment. Applicants respectfully traverse this rejection.

The Examiner cites Anderton, et al. for supporting his position that applicants have not enabled giving muteins, i.e., "altered peptide ligands" to patients with Sjögren's syndrome. The Examiner cites Anderton as concluding that APL's should not be used to treat autoimmune disorders and that in some cases, such an approach may aggravate rather than reduce the disease. (Citing page 370, col. 2, paragraph 1).

In order to expedite allowance of the claims, Applicants have deleted reference to "mutein" and "substantially similar" sequences from claim 14. Based on the Examiner's comments, claim 14 is now allowable.

New claim 27 is directed to muteins of α-fodrin and fragments thereof wherein the mutein is immunochemically equivalent to α-fodrin comprising the amino acid sequence represented by SEQ ID NO: 1. This new claim is supported throughout the specification, e.g., page 7, lines 11-15, lines 28-34; page 8, lines 7-11; page 9, lines 1-5, and thus does not add new matter. These muteins, and the use of the muteins in

the methods of the present invention, are fully enabled by the specification. The Applicants provide sufficient information for one of ordinary skill in the art to make and use the muteins presently claimed in claim 27 without undue experimentation. See e.g., pages 9, line 1 to page 12, line 1 of the application. The amount of guidance necessary to enable the invention is inversely related to the amount of knowledge and predictability in the state of the art. In light of the fact that the amount of knowledge in the art is high, the Applicants have provided substantial guidance within the specification to clearly enable the claimed invention. One of ordinary skill in the art can readily mutate, substitute, delete or insert amino acids into the α-fodrin protein and determine whether the mutein is immunochemically equivalent to α-fodrin without undue experimentation. Such manipulations, while complex, are typically performed by one of ordinary skill in the art. See MPEP 2164.01.

Applicants respectfully disagree with the Examiner's interpretation of the Anderton reference. It is the Applicants understanding that the Examiner should not consider Anderton as it has a date (2001) that is after the filing date of the present application (February 8, 2000, with priority back to 1996). The only time this is proper is if the reference provides evidence of what one skilled in the art would have known on or before the effective filing date of the patent application, or if it showed that the invention was not possible. Anderton fails to meet either criterion.

Furthermore, Anderton et al. used a specific model to study TCR antagonism (MPA (Ac1-9) model of EAE) and found that APL based therapy, for TCR antagonists and Th2 immune responses, is complicated by certain factors such as the complexity of T-cell responses, unpredictability if APL effects and harmful hyper-reactivity to the APL. See e.g., page 370, col. 2. However, contrary to the Examiner's interpretation of Anderton et al., the reference also states that APLs may also be useful for improving the efficacy of soluble peptide therapy. For example, APLs may be used to increase the affinity for the peptide for MHC. (See e.g., page 373, middle of column 1 and last paragraph in column 2.) Thus, in contrast to the Examiner's position that the use of α-fodrin muteins is non-enabled, the citing of the reference actually supports the applicants' position that one of ordinary skill in the art would be enabled to use α-

fodrin muteins to prevent or treat Sjögren's syndrome in accordance with the methods of the present invention.

Furthermore, Applicants would like to point out that the term "mutein" is commonly used in issued U.S. patents. For example, Applicants direct the Examiner's attention to Patent No. 6,083,919, which claims:

> 1. A method for treating Multiple Sclerosis (MS) in a patient in need of such treatment, said method comprising administering a synergistically effective amount of IL-10 and TGF-β, or a biologically active mutein, fragment, variant or peptide thereof, to said patient.

See also claims 7 and 14. A copy of this patent is enclosed for the Examiner's reference. The muteins are described at column 4, lines 8-16 of Patent No. 6,083,919. This is far less enablement than that provided by Applicants. Thus, the present application provides sufficient enablement to one of ordinary skill in the art to prevent or treat Sjögren's syndrome by administering to a patient a therapeutically effective amount of a mutein of α-fodrin, or a fragment thereof.

Applicants respectfully submit that the scope of the claims covering this invention should include the use of muteins of α-fodrin because one of ordinary skill in the art can readily make and use these muteins.

Therefore, Applicants respectfully request that this rejection be reconsidered and withdrawn.

In view of the above discussion and amendment, it is respectfully submitted that the present application is in condition for allowance. Therefore, an early reconsideration and allowance are respectfully requested.

Should the Examiner wish to discuss any of the amendments and/or remarks made herein, the undersigned attorney would appreciate the opportunity to do so.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE.

IN THE CLAIMS

Please amend the claims as follows:

14. (twice amended) A method for preventing or treating Sjögren's syndrome which comprises administering to a patient a therapeutically effective amount of

α-fodrin, ~~a mutein thereof,~~

an antigenic fragment available upon proteolysis of α-fodrin with a protease, which ~~contains or~~ comprises an amino acid sequence ~~substantially shown by Arg-Gln-Lys-Leu-Glu-Asp-Ser-Tyr-Arg-Phe-Gln-Phe-Phe-Gln-Arg-Asp-Ala-Glu-Glu-Leu (SEQ ID NO:1)~~ represented by SEQ ID NO:1, or

a salt thereof, ~~and the~~

wherein the α-fodrin or antigenic fragment has a molecular weight of ~~which is~~ from about 2K to about 240K~~, or a salt thereof with a pharmaceutically acceptable carrier~~.

Please cancel claim 25, without prejudice.

Please add the following new claims:

--26. The method of claim 14, wherein the molecular weight of said α-fodrin or antigenic fragment is from about 100K to about 140K.

27. A method for preventing or treating Sjögren's syndrome which comprises administering to a patient a therapeutically effective amount of

a mutein of α-fodrin,

an antigenic fragment thereof available upon proteolysis of α-fodrin with a protease,

or a salt thereof,

wherein the α-fodrin or antigenic fragment has a molecular weight of from about 2K to about 240K and wherein the mutein is immunochemically equivalent to α-fodrin comprising the amino acid sequence represented by SEQ ID NO:1.--